Anaemia and patient blood management in patients having neck dissections or free flaps for head and neck cancer

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The paper has not be presented at any meeting except at our regional audit day. The study approved by the Clinical Audit Department at Aintree University Hospital. There is no conflict of interest.

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Introduction

The World Health Organisation (WHO) defines iron deficiency anaemia as Hb<130 g/L in men older than 15 years and <120 g/L in non-pregnant women older than 15 years. [1] The commonest haematological abnormality in HNC patients at presentation is anaemia, usually from iron deficiency. [2] Reasons could include difficulties with nutrition due to dysphagia, poor diet, and life style (particularly high alcohol intake). With microvascular reconstruction following tumour ablation it is considered acceptable for haemoglobin levels to fall during surgery through blood loss and haemodilution, as reduced blood coagulability can help anastomosis success. Consequently, anaemia does occur intra-operatively and since peri-operative blood transfusions (PBT) are avoided where possible, post-operative anaemia is common. This anaemia could contribute to poorer wound healing, fatigue, delayed recovery and worse health related quality of life. During follow-up around one fifth of patients report fatigue/tiredness. [3]

A meta-analysis of 4984 patients from 28 articles, indicated preoperative anaemia as a potential risk factor for free flap failure, with postoperative transfusion associated with more medical complications. [4] Anaemia (< 12 g/dl) at different treatment times (pre and postoperative, before and during radiotherapy) was reported as an independent negative prognostic factor for local recurrence-free and overall survival in HNC patients. [5] Similar findings were reported by van de Pol et al. [6] Anaemia and BMI independently predicted overall survival for laryngeal SCC [7], whilst in oropharyngeal cancer, treated mainly by surgery, comorbidity and anaemia significantly influenced disease specific survival and had more impact on overall survival than p16 status. [8]

Peri-operative blood transfusion (PBT) rates in HNC free flap patients vary across units, for example from one quarter [9] to nearly half. [10] One reason for this are differences in criteria for when to transfuse. Rossmiller [11] suggested a postoperative transfusion trigger of haematocrit < 25 percent which decreases blood transfusion rates without increasing flap-related complications. Clinical characteristics such as body mass index, tumour stage, preoperative haemoglobin level, and type of free-flap reconstruction have been identified as associates of PBT and can be used to inform risk stratification. [9,12,13] Occasionally a PBT is required for patients only having a neck dissection (ND). [14]

Every effort should be made to limit the amount of blood transfused as PBT carries risk. Patients receiving three or more units of blood after free tissue transfer for HNC were

reported as having significantly worse prognosis (survival, wound infection), [15,16] even after controlling for age, preoperative haemoglobin and albumin, cancer stage, and adverse pathologic features. The precise mechanism is unclear but might relate to an altered immunological response. [17] Fenner et al [18] reported that transfusion of >4 Units of blood did not appear to influence overall survival as the strongest predictors were age and ASA class. Other salient reasons to limit PBT relate to shortage of blood donations and expense.

United Kingdom Multidisciplinary guidelines recommend that intravenous iron should be considered for anaemia in the urgent HNC patient, that preoperative blood transfusion should be avoided where possible, and when essential it should be completed 24–48 hours pre-operatively. [2] There are also NICE guidelines for blood transfusion that are relevant. [19, 20] Though not specific to head and neck cancer and reconstructive microsurgery, the essence of these are, firstly that people with iron-deficiency anaemia who are having surgery are offered iron supplementation before and after surgery. Secondly, adults having surgery and expected to have moderate blood loss are offered tranexamic acid. Thirdly, people have their haemoglobin levels checked after each unit of red blood cells they receive, unless they are bleeding or are on a chronic transfusion programme.

Hence there were two main study aims. Firstly, to audit haemoglobin levels peri-operatively, from pre-operative assessment to ward post-operative discharge, in patients having neck dissection or microvascular free tissue reconstruction for HNC. Secondly to audit which patients had blood transfusions, and the compliance against national transfusion guidelines.

Patient and Methods

Patients having neck dissection or microvascular free tissue reconstruction for HNC from October 2016 to September 2017 at Aintree Hospital Regional Maxillo-Facial Unit were included. There were no exclusion criteria. Cases were identified from theatre lists. Electronic patient records were used to access operation notes, blood prescription and results, discharge medication and first clinical outpatient review.

The study was approved by the Clinical Audit Department at Aintree University Hospital.

Fishers exact test was used to compare categorical data between patient groups. The Mann-Whitney test (2 group comparison) or Kruskal-Wallis test (>2 group comparison) was used to compare numerical data between patient groups. Statistical significance was at the 5% level. Analyses were performed using SPSS version 25.

Results

There were 131 surgical patients, involving soft free-flaps for 50% (65), hard free-flaps for 26% (34) and neck dissection only for 24% (32). For neck dissection patients, at a median (IQR) of 18 (12-28) days before surgery the median (IQR) pre-op Hb was 147 (136-157) g/L, n=28, range 118-185 g/L. Most (25/32) were admitted on the day of surgery, and at a median of 1 (0-2) days before discharge had a median (IQR) Hb of 131 (119-144) g/L, n=26, range 104-163 g/L. Using the WHO definition of anaemia 4% (1/28) were anaemic pre-operatively and 42% (11/26) on discharge. No neck dissection patient received a blood transfusion and none were discharged on iron. Group and save was first performed at a median (IQR) of 11 (1-15) days and the second at 0 (0-1) days before surgery, n=25. The remainder of the results relates to free-flap surgery.

Median (IQR) age of the 99 free-flap surgery patients was 66 (57-72) years, 61 male and 38 female. Three-quarters (74) had oral cancer, 8 oropharyngeal cancer, 5 ORN and 12 other. Staging was early (0-2) for 30, late (3-4) for 61, unknown for 8. Neck location was unilateral for 62, bilateral for 18 with vessel access for 19. Seven patients were in the AMG 319 trial. [21]

At 3-4 weeks before surgery on average, one in five patients were anaemic (Table 1), with 3 patients below 110g/L. Twelve of 16 anaemic patients were aged 70 years or more; 41% (12/29) aged ≥70 were anaemic, 8% (2/26) aged 60-69, 7% (2/30) aged <60, P=0.001. On admission 47% of hard free-flap and 27% of soft free-flap patients were anaemic (P=0.10, Fishers exact test). Two patients (1 hard, 1 soft) had Hb levels <100 g/L on admission and six more had an Hb of 100-109 g/L. The first Group and Save was a median of 6 days before surgery and the second of 1 day before surgery. Haematinic deficiency checks were documented in 7% (7/99) of patients (3 hard, 4 soft) before surgery; one patient was put on folic acid, no action was taken for one, otherwise unknown.

Hb levels fell by around 30 g/L on average from admission to during surgery (Table 1). Intra-operative Hb fell below 80g/L for 14% (12/84), 80-89 g/L for 19% (16/84) and 90-99 g/L for 19% (16/84). Almost all (98%) were anaemic. Four patients received tranexamic acid during surgery. There were surgical complications for 13% (13/99). Three-quarters (77%, 10/13) of patients with complications received one or more RBC transfusion, compared with 19% (16/86) without complications (P<0.001, Fishers exact test). One patient (hard free-flap) died

in ITU. Other issues were haematoma evacuation (5), flap failure (4), flap salvage (1), bleeding/tracheostomy (1), blowout & haematoma evacuation (1).

Post-surgery Hb changed little until discharge (Table 1). Discharge prescriptions (TTO's) for iron were issued to 24% (8/33) hard and 23% (15/65) soft free-flap patients. Median (IQR) last Hb for patients discharged on iron was 93 (77-103) g/L, n=23 and was 103 (94-114) g/L, n=75 if not on iron, P=0.005 Mann-Whitney test. All 7 patients with last Hb <80 g/L were prescribed iron, 22% (2/9) if 80-89 g/L, 18% (6/33) if 90-99 g/L, 24% (5/21) if 100-109 g/L and 11% (3/28) if ≥110 g/L. Hb levels were reviewed at the next appointment for 18% (16/90), unknown for 8 followed elsewhere and reviews were mainly opportunistic.

Forty-one red blood cell transfusions (61 units) were received by 26% (26/99), 35% (12/34) hard free-flap and 22% (14/65) soft free-flap. Most (61%, 26/41) transfusions were single unit, with 27% (11) transfused two units, 7% (3) three units and 2% (1) four units. Four transfusions were before surgery, 29% (12) on the day of surgery, 32% (13) the day after, 15% (6) two days after, 10% (4) 3-8 days after, and two after 19 and 31 days. Hb checks after each RBC unit were known for 39 transfusions (24 patients) and were done for 79% (31/39); 33% (8/24) of patients had a transfusion episode without such a check, 2 with surgical complications. Twelve of the 39 transfusions were given during surgery with Hb checks for all. In addition to RBC transfusion, one (hard free-flap) patient received one unit of platelets and four units of fresh frozen plasma (FFP), and another (soft free-flap) received five units of FFP.

Two patients were <100 g/L on admission and were transfused. One (soft ALT free-flap) was admitted 13 days before surgery (Hb 77 g/L) and was transfused two RBC units 9 days before surgery, one RBC unit 8 days before surgery and one unit the day after surgery. The other (hard DCIA free-flap) patient was admitted one day before surgery (Hb 81g/) and received two RBC units on admission day and two more units on the day of surgery. One other patient was transfused before surgery, being admitted (Hb 120 g/L) for bleeding/tracheostomy; two RBC units were given 10 days before surgery with one further unit on the day of surgery. The patient transfused 31 days after surgery was given four RBC units three days after a second operation. The patient transfused 19 days after surgery had a lowest ward Hb of 71 g/L and was transfused on the day of discharge. Transfusions during days 3-8 after surgery were for patients already previously transfused since surgery.

RBC transfusion was more strongly associated with lowest Hb during ITU than with admission or lowest intra-operative Hb (Table 2). Hb levels were more comparable by discharge (Table 3). The relation observed between lowest ITU, lowest ward and discharge Hb is shown in Table 4. Seven patients (7%) had last Hb levels <80 g/L and 4 of these had similar levels during their stay in ITU and all 7 during their ward stay. Two of these 7 patients received one RBC unit one day after surgery and all 7 were prescribed iron on discharge. Another 9% (9) had a last Hb of 80-89 g/L.

Admission Hb was significantly lower for females and for patients with late tumours (Table 5). None of the clinic-demographic variables measured were significantly associated with change in Hb from admission to the lowest recorded during surgery nor between admission and discharge. Other than discharge Hb levels being significantly lower for hard free-flap surgery, no associations were observed. There were no statistically significant associations with being transfused, though it was observed that hard free-flap patients and later stage patients were transfused more often (Table 6). Females were more likely to be prescribed iron on discharge as were non-oral cancer patients.

Discussion

Anaemia and blood management in HNC patients is important since they relate to complications, survival and quality of life. In surgical settings anaemia can be managed by peri-operative blood transfusion (PBT), though not without risk. This retrospective case note review detailed Hb levels in patients having neck dissection and free flaps and comprises a consecutive contemporaneous sample but is limited in terms of being from a single institution. The findings have highlighted potential deficits in management and have allowed opportunities to reflect on how to improve. Neck dissection was included for comparative purposes and also because our current practice is to group and save and this carries cost implications.

About one fifth of free-flap patients were anaemic at pre-operative assessment, and rates were highest in the elderly. Average time from pre-op assessment to operation was about three weeks, and as haemoglobin continues to fall in this period (on average 7-8 g/L) there is ample opportunity to administer IV iron (IVI). This strategy would comply with statement 1 of NICE guideline QS138. [19]

Around a 30g/L drop in Hb was seen for free-flap patients from admission to after operation. To reduce blood loss during resection we have now made it our practice to administer tranexamic acid (TXA) at the time of tumour ablation and so far TXA has been safe to use and has not comprised flap success. Although early findings are very positive this is the subject on an ongoing audit. TXA can significantly reduce blood loss and chances of colloid, blood, and crystalloid transfusion caused by HNC surgery. [22] However, in another study TXA did not reduce intraoperative blood loss or need for transfusions. [23] The use of TXA complies with statement 2 of NICE guideline QS138. [19]

Patients only having neck dissection (ND) usually present with higher Hb on admission and in this series no PBT was given. Discharge Hb levels were satisfactory and there was little indication for iron supplements. Very occasionally it will be necessary to give a PBT for patients having neck dissection. [14]

One quarter of free-flap patients were transfused, mostly intra-operatively or in the first few days post-operatively. The local hospital recommendation is for patients only to have a blood transfusion in theatre or the high dependency unit if Hb falls below 90 g/L. Depending on the individual patient this might fall as low as 80 g/L and only then would patients definitely be given a transfusion. Most patients only had one unit of blood given and most had their haemoglobin levels checked after each unit of red blood cells. However, there is room for improvement regarding compliance with statement 3 of NICE guideline QS138.[19]

The post-operative fall in Hb for free flap patients remained until discharge. There is evidence for correcting such anaemia, particularly for those having radiotherapy or chemotherapy, as anaemia has been shown as an independent significant prognostic factor in survival [24] and might relate to tumour cell oxygenation. Levels <12 g/dl were associated with worse outcomes. [25] There is merit in giving IV iron during the post-operative in-patient stay. In our sample in spite of the frequency of post-operative anaemia only a quarter of patients were prescribed oral iron, due to concerns regarding its efficacy.

In conclusion this cohort has highlighted the issue of blood loss and anaemia in patients having HNC tumour ablation associated with free tissue reconstruction. In respect of blood transfusion guidelines there were two areas that raised particular concern, namely the use of TXA and IVI. As post-operative anaemia is common IVI should be used where possible instead of blood transfusion and TXA should be given as part of resection management. Table 7 summarises a proposed schema for patients with head and neck cancer undergoing

microvascular reconstruction. The patient benefit of these require further investigation but could lead to improved outcomes such as a reduction in complications, lower levels of fatigue and improved HRQOL.

Conflict of interest statement

We have no conflicts of interest.

Ethics statement/confirmation of patient's permission

The data, which had been collected as part of a service audit rather than for research, met the criteria of the local Clinical Governance Department for service evaluation.

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Table(s)

Table 1. Haemoglobin levels before, during and after surgery.

	Hard Free-flaps (N=34)			Soft Free-flaps (N=65)		
	Median (IQR) Days from surgery	Median (IQR) Hb g/L	WHO definition of anaemia*	Median (IQR) Days from surgery	Median (IQR) Hb g/L	WHO definition of anaemia*
Pre-op 1st Group & Save** 2nd Group & Save	-22 (-31, -8), n=33 -6 (-14, -2), n=32 -1 (-1, -1), n=32	135 (128-145), n=28	21% (6/28)	-27 (-39, -12), n=61 -6 (-23, -1), n=54 -1 (-1, -1), n=60	137 (129-147), n=57	18% (10/57)
Admission	1 (-1, -1), n=34	127 (120-134), n=30	47% (14/30)	1 (-1, -1), n=64	130 (124-141), n=62	27% (17/62)
Intra-op		93 (86-103), n=28	96% (27/28)		103 (86-113), n=56	98% (55/56)
ITU lowest		89 (82-96), n=34	100% (34/34)		98 (86-108), n=65	100% (65/65)
Ward lowest	6 (4-7), n=33	91 (86-96), n=33	100% (33/33)	3 (3-7), n=63	96 (85-103), n=65	100% (65/65)
Last Hb	7 (7-13), n=33	95 (90-104), n=33	97% (32/33)	7 (4-13), n=65	103 (95-114), n=65	98% (64/65)
Discharge	10 (8-14), n=33			9 (6-14), n=65		

*Males Hb<130 g/L, Females Hb<120 g/L

** a further 12 (2 hard, 10 soft) 'had history' while 1 (soft) had 'none' taken.

Table 2 Red Blood cell transfusion in relation to Haemoglobin levels at admission, the lowest Hb recorded during surgery and the lowest recorded in ITU

	Hb g/L	Hard free-flaps	Soft free-flaps	All free-flaps	
Admission	<70	-	-	-	-
	70-9	-	1/1	100%	1/1
	80-9	1/1	-	100%	1/1
	90-9	-	-	-	-
	100-109	2/2	3/4	83%	5/6
	110-119	2/4	2/5	44%	4/9
	120-129	4/13	6/19	31%	10/32
	130+	2/10	1/33	7%	3/43
	Not known	1/4	1/3	29%	2/7
Lowest during surgery	<70	-	1/1	100%	1/1
	70-9	3/4	7/7	91%	10/11
	80-9	2/6	4/10	38%	6/16
	90-9	1/9	0/7	6%	1/16
	100-109	2/6	1/15	14%	3/21
	110-119	0/2	1/10	8%	1/12
	120-129	-	0/6	0%	0/6
	130+	1/1	-	100%	1/1
	Not known	3/6	0/9	20%	3/15
Lowest in ITU	<70	1/1	-	100%	1/1
	70-9	6/6	3/5	82%	9/11
	80-9	5/11	7/12	52%	12/23
	90-9	0/11	4/19	13%	4/30
	100-109	0/3	0/18	0%	0/21
	110-119	0/2	0/8	0%	0/10
	120-129	-	0/3	0%	0/3
	130+	-	-	-	-
	Not known	-	-	-	-

Table 3: Haemoglobin levels by whether or not patient was transfused.

	Transfusion group Median (IQR) Hb g/L	No-Transfusion group Median (IQR) Hb g/L	P value*
Pre-op	125 (117-135), n=19	138 (132-150), n=66	<0.001
Admission	122 (109-127), n=24	133 (126-141), n=68	<0.001
Intra-op	82 (75-90), n=22	104 (92-114), n=62	<0.001
ITU lowest	83 (76-87), n=26	98 (92-108), n=73	<0.001
Ward lowest	90 (82-96), n=25	96 (87-103), n=73	0.01
Last Hb	98 (92-108), n=25	102 (92-113), n=73	0.45

*Mann-Whitney test

Table 4. Lowest Haemoglobin level recorded in ITU by last reading taken closest to discharge

	Last Hb (g/L) closest to discharge							
	70-9	80-9	90-9	100-109	110-119	120-129	130+	Total
Lowest Hb (g/L) in ITU								
<70	-	-	-	1	-	-	-	1
70-9	4	-	4	2	-	-	-	10
80-9	3	4	10	1	3	-	2	23
90-9	-	5	13	8	4	-	-	30
100-109	-	-	5	8	8	-	-	21
110-119	-	-	1	1	3	5	-	10
120-129	-	-	-	-	2	1	-	3
Total	7	9	33	21	20	6	2	98
Lowest Hb (g/L) in ward								
70-9	7	3	1	1	1	-	-	13
80-9	-	6	11	2	2	-	-	21
90-9	-	-	21	9	6	-	2	38
100-109	-	-	-	9	6	1	-	16
110-119	-	-	-	-	5	3	-	8
120-129	-	-	-	-	-	2	-	2
Total	7	9	33	21	20	6	2	98

Table 5. Haemoglobin levels in relation to patient and clinical characteristics

		Median (IQR) Admission Hb (g/L)	P value*	Median (IQR) Decrease in Hb (g/L) from admission to Lowest during surgery	P value*	Median (IQR) Decrease in Hb (g/L) from admission to discharge	P value*	Median (IQR) Last Hb (g/L)	P value*
All patients		129 (122-140), n=92		30 (20-40), n=78		29 (18-38), n=91		100 (92-111), n=98	
Surgical group	Hard Free-flap	127 (120-134), n=30	0.10	32 (25-40), n=24	0.36	32 (23-37), n=29	0.41	95 (90-104), n=33	0.005
	Soft Free-flap	130 (124-141), n=62		30 (17-42), n=54		27 (17-38), n=62		103 (95-114), n=65	
Gender	Male	134 (125-141), n=55	0.005	32 (24-43), n=46	0.07	30 (22-39), n=54	0.23	102 (93-113), n=60	0.30
	Female	126 (120-131), n=37		24 (17-39), n=32		27 (12-36), n=37		98 (91-109), n=38	
Age	<60	127 (121-140), n=34		30 (18-37), n=30	0.56	27 (14-40), n=34	0.11	98 (91-113), n=36	
	60-69	134 (126-140), n=31	0.25	31 (24-43), n=24		34 (24-39), n=31		102 (91-110), n=31	0.87
	≥70	128 (120-140), n=27		28 (17-43), n=24		28 (18-33), n=26		102 (92-113), n=31	
Diagnosis	Oral	129 (123-140), n=68		30 (19-39), n=58		29 (19-38), n=67		102 (91-112), n=73	
	Oropharyngeal	130 (na), n=8	0.55 oral Vs rest	34 (na), n=7	0.37 oral Vs rest	30 (na), n=8	0.90 oral Vs rest	105 (na), n=8	0.81 oral Vs rest
	ORN	129 (na), n=5		34 (na), n=5		31 (na), n=5		97 (na), n=5	
	Other	124 (120-140), n=11		30 (na), n=8		28 (22-37), n=11		95 (80-113), n=12	
Stage	Early	133 (126-143), n=29	0.05	31 (22-44), n=23	0.56	29 (20-38), n=29	0.81	105 (95-115), n=30	0.14
	Late	127 (121-139), n=55	excl NK	30 (18-40), n=47	excl NK	29 (21-38), n=54	excl NK	99 (90-110), n=60	excl NK
	NK	122 (na), n=8		29 (na), n=8		24 (na), n=8		98 (na), n=8	
Neck	Unilateral	129 (124-140), n=58		28 (18-40), n=48	0.33	32 (22-38), n=57	0.58	100 (91-113), n=61	
	Bilateral	129 (123-141), n=17	0.60	36 (21-49), n=15		26 (12-39), n=17		103 (98-111), n=18	0.22
	Vessel access	127 (119-137), n=17		33 (22-41), n=15		28 (16-39), n=17		95 (91-106), n=19	

*Mann-Whitney (2 group comparison) or Kruskall-Wallis (>2 group comparison) test
Also Note: (na) refers to IQR not being given as there was <10 cases

Table 6 Red Blood Cell transfusion and prescription of iron on discharge, in relation to patient and clinical characteristics

		% (n) with RBC transfusion	P value*	% (n) prescribed iron on discharge	P value*
All patients		26% (26/99)		23% (23/98)	
Surgical group	Hard Free-flap	35% (12/34)	0.16	24% (8/33)	>0.99
	Soft Free-flap	22% (14/65)		23% (15/65)	
Gender	Male	23% (14/61)	0.36	17% (10/60)	0.05
	Female	32% (12/38)		34% (13/38)	
Age	<60	25% (9/36)		19% (7/36)	
	60-69	26% (8/31)	0.96	26% (8/31)	0.80
	≥70	28% (9/32)		26% (8/31)	
Diagnosis	Oral	23% (17/74)		18% (13/73)	
	Oropharyngeal	50% (4/8)	0.29 Oral	38% (3/8)	0.03 Oral
	ORN	60% (3/5)	Vs Rest	20% (1/5)	Vs rest
	Other	17% (2/12)		50% (6/12)	
Stage	Early	17% (5/30)	0.30 excl	13% (4/30)	0.30 excl
	Late	28% (17/61)	NK	28% (17/60)	NK
	NK	50% (4/8)		25% (2/8)	
Neck	Unilateral	24% (15/62)		23% (14/61)	
	Bilateral	28% (5/18)	0.76	17% (3/18)	0.59
	Vessel access	32% (6/19)		32% (6/19)	

*Fishers exact test

Table 7; Proposed schema for patients with head and neck cancer undergoing microvascular reconstruction

Pre-operative	• Early pre-operative bloods to identify patients with iron deficiency anaemia. Ideally immediately following the consultation at which treatment planned agreed. Haemocue can help rapid identification of anaemia. • If Hb less than 120 consider administration of IV iron as soon as possible before planned operation date • Re-check Hb two weeks later, assess need for second treatment, though if close to time of surgery it will be likely that there will be a need for peri-operative transfusion or IV iron post-operatively
Intra-operative	• Optimal surgical techniques to avoid blood loss • Hypotensive anaesthesia • Hourly assessment of blood loss and Hb checks • Administration of 1 gram tranexamic acid at start of resection • Consider cell salvage • Use of single unit transfusions unless massive unexpected blood loss
Post-operative	• The use of blood transfusion will depend on unit protocols and individual patient considerations • If Hb less than 120 at day two / three consider IV iron • Avoid use of oral oral iron – low efficacy and side-effects • Check Hb prior to discharge and review in first consultation post-discharge. If less that 120 consider repeat IV iron if two weeks following the most recent infusion

Anaemia and patient blood management in patients having neck dissections or free flaps for head and neck cancer

Rogers SN, Horisk K, Groom P, Lowe D

Conflict of interest statement

We have no conflicts of interest.

Ethics statement/confirmation of patient's permission

The data, which had been collected as part of a service audit rather than for research, met the criteria of the local Clinical Governance Department for service evaluation.

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Please provide details in the table below of each author(s) contribution to the submitted manuscript

AUTHORS	Conception and design of study/review/case series	Acquisition of data: laboratory or clinical/literature search	Analysis and interpretation of data collected	Drafting of article and/or critical revision	Final approval and guarantor of manuscript
Rogers	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**
Horisk		**Yes**		**Yes**	
Groom	**Yes**			**Yes**	
Lowe	**Yes**		**Yes**	**Yes**	

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CONFIRMATION OF AUTHORSHIP

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We, the undersigned, confirm that we are the joint authors of the above paper.

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We confirm that, to our knowledge, all the claims, statements and conclusions are true and are our jointly held opinions.

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